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(71) Applicant (for all designated States except US): **THE TRUSTEES OF BOSTON UNIVERSITY [US/US]; 147 Bay State Road, Boston, MA 02215 (US).**
(72) Inventors; and
(75) Inventors/Applicants (for US only): **WAXMAN, David, J. [US/US]; 30 Clements Road, Newton, MA 02458 (US). SCHWARTZ, Pamela, S. [US/US]; 7201 Seward Park Avenue S., Seattle, WA 98118 (US).**

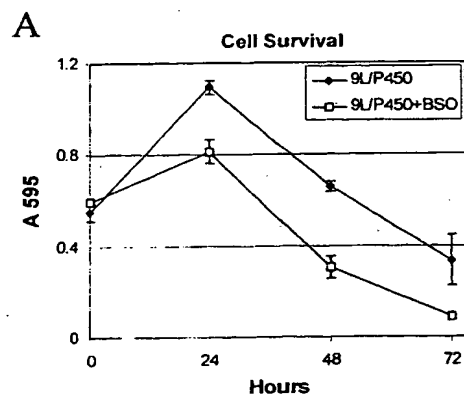
(74) Agents: **EISENSTEIN, Ronald, I. et al.; Nixon Peabody LLP, 101 Federal Street, Boston, MA 02110 (US).**

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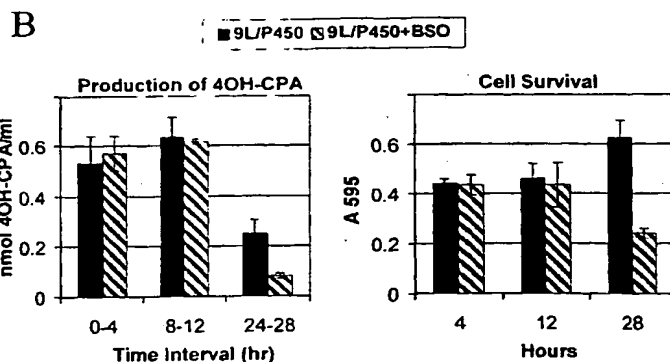
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[Continued on next page]

(54) Title: METHOD OF USING ANTI-APOPTOTIC FACTORS IN GENE EXPRESSION



(57) Abstract: The present invention is directed to methods of prolonging the expression of a heterologous gene (transgene) in a cell, preferably a malignant cell. This method can be used to increase the concentration of a chemotherapeutic agent in a target cellular environment. Preferably, the present invention relates to methods of inhibiting apoptotic cell death to enhance transgene expression, such as gene-directed enzyme/prodrug therapy.



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J. [US/US]; 30 Clements Road, Newton, MA 02458 (US).
SCHWARTZ, Pamela, S. [US/US]; 7201 Seward Park Avenue S., Seattle, WA 98118 (US).

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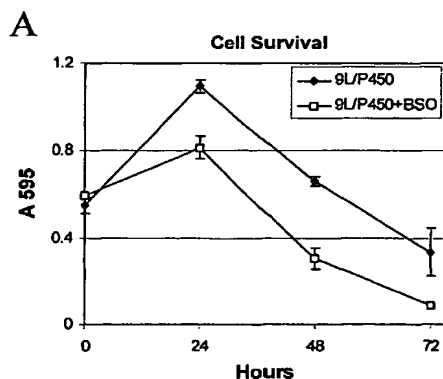
(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,

(72) Inventors; and

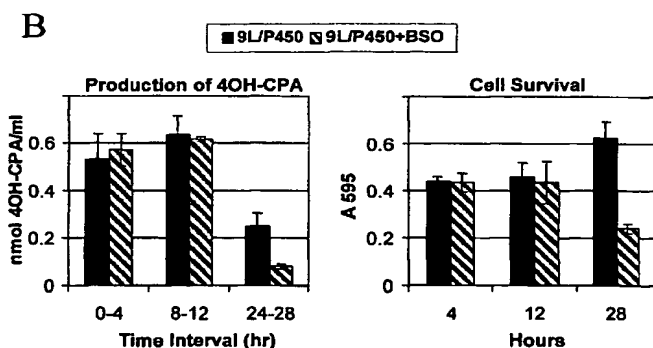
(75) Inventors/Applicants (for US only): **WAXMAN, David**,

[Continued on next page]

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INTERNATIONAL SEARCH REPORT

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PCT/US03/08743

A. CLASSIFICATION OF SUBJECT MATTER												
IPC(7) : A61K 31/70; C12N 15/63; C07H 21/04												
US CL : 514/44; 435/320.1, 455; 536/23.2, 23.4, 23.7												
According to International Patent Classification (IPC) or to both national classification and IPC												
B. FIELDS SEARCHED												
Minimum documentation searched (classification system followed by classification symbols) U.S. : 514/44; 435/320.1, 455; 536/23.2, 23.4, 23.7												
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched												
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet												
C. DOCUMENTS CONSIDERED TO BE RELEVANT												
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.										
X	WO 98/46637 A2 (ARCH DEVELOPMENT CORPORATION) 22 October 1998, see pages 34-38 under the section Methods for the inhibition of apoptosis.	1										
Y		2										
Y	US 6,207,648 B1 (WAXMAN et al) 27 March 2001, see abstract and claims.	2										
Y	US 5,688,773 A (CHIOCCA et al) 18 November 1997, see abstract and claims.	2										
X,P	SCHWARTZ et al. Enhanced bystander cytotoxicity of P450 gene-directed enzyme prodrug therapy by expression of the antiapoptotic factor p35. Cancer Research. 01 December 2002, Vol. 62, pages 6928-6937, see the entire document, especially the abstract.	1-35										
A	US 6,156,535 A (KORNELUK et al) 05 December 2000, see cols. 17-19.	1-35										
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.												
* Special categories of cited documents: <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</td> </tr> <tr> <td>"E" earlier application or patent published on or after the international filing date</td> <td>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td> </tr> <tr> <td>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</td> <td>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"&" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	"P" document published prior to the international filing date but later than the priority date claimed	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention											
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"P" document published prior to the international filing date but later than the priority date claimed												
Date of the actual completion of the international search 04 November 2003 (04.11.2003)		Date of mailing of the international search report 18 DEC 2003										
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230		Authorized officer <i>Quang Nguyen, Ph.D.</i> Telephone No. (703) 308-0196										

INTERNATIONAL SEARCH REPORT

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Continuation of B. FIELDS SEARCHED Item 3:

APS, DIALOG, MEDLINE, EMBASE, BIOSIS, CANCER LIT.

Search terms: antiapoptotic, apoptosis inhibiting, inhibitor of apoptosis, prodrug therapy, GDEPT, enhanced, increased therapeutic, bystander.